In Vivo Effects of Right Cervical Vagus Nerve Stimulation on Salt Induced Hypertensive Heart Disease Rats

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Introduction

- Vagal nerve stimulation (VNS) can restore the autonomic nervous system balance in the vascular system and in the heart to reduce risk of heart failure from hypertension (HTN).
- The potential of VNS to be used as a novel device-based therapy for HTN and HTN-induced heart diseases. The effect of VNS on mean arterial blood pressure (MAP) and arrhythmogenesis *in-vivo* in a genetic model of hypertension was studied.

Methods

EXPERIMENT TIMELINE

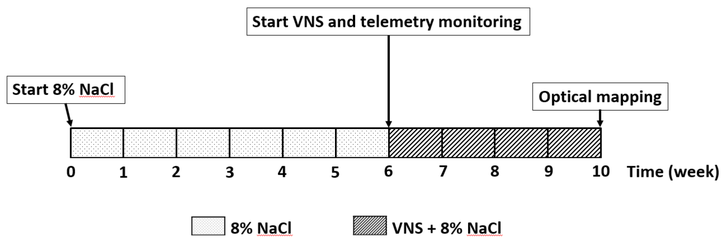


Figure 1. Timeline of study that shows VNS was introduced in the subjects from week 7 to week 10.

ANIMAL MODEL

Subjects used were dahl salt sensitive rats that was fed with high salt diet to induce hypertension

Vagal nerve stimulators (Cyberonics Model 103, Houston, TX, USA) and DSI transmitters (HD-S11, DSI Inc., MN, USA) implanted at the beginning of the study

•Rats were randomly divided into 2 groups: HTN-Sham (n=6, with non-functional VNS stimulators) and HTN-VNS (n=6, with functional VNS stimulators).

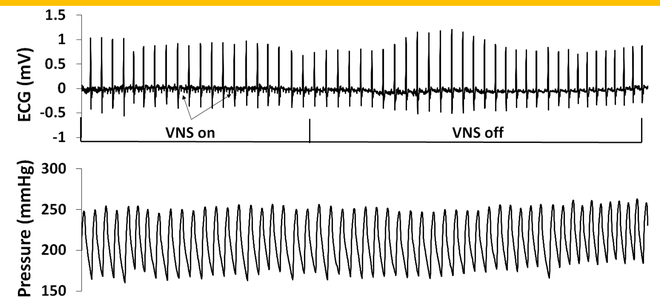
•Real time electrocardiography (ECG) and arterial blood pressure data were monitored *in-vivo* and compared

•Functional vagal nerve stimulators were subdermally implanted in the HTN-VNS rats at the right cervical vagus nerve .

•Pressure catheter was implanted into the descending aorta. The real time ECG and mean arterial blood pressure (MAP) data were collected with 500 Hz sample rate.

Methods (cont.)

VNS STIMULATION



Parameters:
- Frequency: 20 Hz
- Pulse width: 500 µsec
- Current: 1mA
- Duty Cycle: 12%

Figure 2. Shows the difference in small artifacts in the ECG recording when VNS stimulation is turned on. VNS stimulation had no effects on the blood pressure recording .

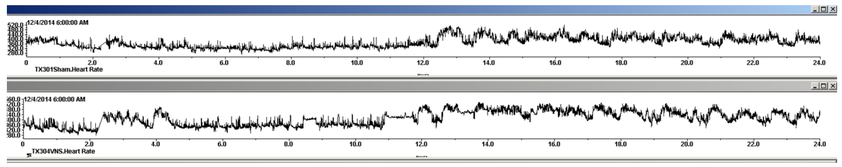


Figure 3. 24 hour heart rate (HR) samples of VNS rats and Sham rats from 6AM to 6AM next day.

Results

AVERAGE MAP

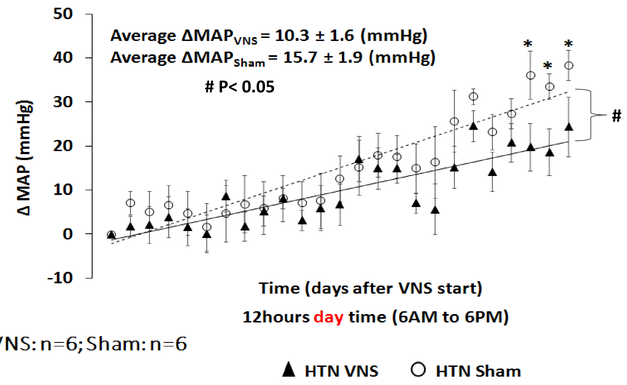


Figure 4. Average MAP values for day time monitoring of VNS rats versus Sham rats

INDUCED HYPERTENSIVE HEART DISEASE

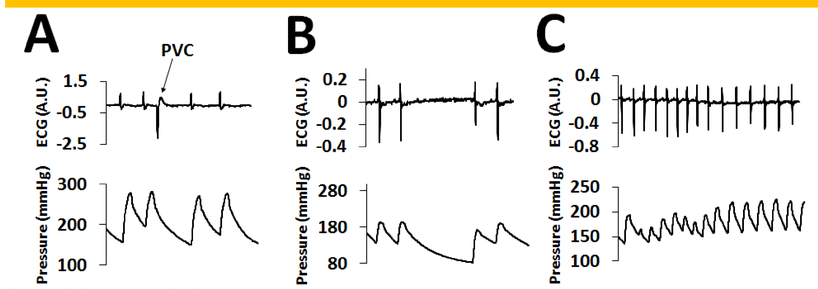


Figure 5. Episodes of PVC and other arrhythmias were observed in rats after the 6 weeks of high salt diet as shown. Typical examples of PVC (Fig. 5A, arrow) and arrhythmias (Fig 5B, skipping beats; Fig 5C, VT) are shown with the corresponding arterial blood pressure trace in the bottom

Results (cont.)

4 WEEKS VNS (ECG) in vivo

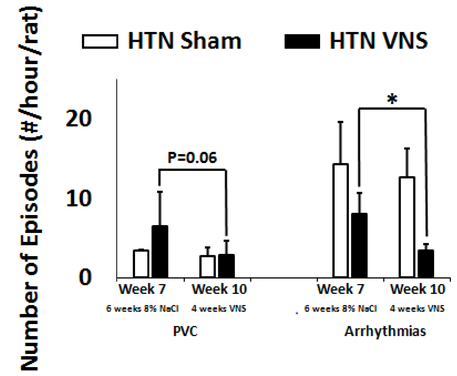


Figure 6. The PVC and arrhythmia were observed in both HTN Sham and HTN VNS rats after first 6 weeks on high salt diet. HTN VNS, but not HTN Sham, rats started to exhibit significantly decreased frequency of the arrhythmias occurrence after 4 weeks of VNS.

Figure 7. The heart weight/tibia length ratio (HW/TL) and RV/LV wall thickness ratio measured showing no induce a structural remodeling of the heart

Conclusions

In this study, we investigated the effects of VNS on arterial blood pressure and ECG during *in-vivo* experiments and the electrical properties of the rat hearts during periodic pacing and VT/VF. We investigated possible mechanisms underlying these effects.

Our results demonstrated two main findings. First, long term (more than 2 weeks) VNS reduced blood pressure and induced anti-arrhythmic effects. Second, These changes are not induced through the structure remodeling mechanism.

Key References

1 Harman M.A., Reeves T.J., "Effects of vagus nerve stimulation on atrial and ventricular function.", Am J Physiol 1968; 215:1210–1217.

2 X.Xie, S.W. Lee, Ch. Johnson, J. Ippolito, B.H. KenKnight, Elena G. Tolkacheva. "Intermittent Vagal Nerve Stimulation Alters the Electrophysiological Properties of Atrium in the Myocardial Infarction Rat Model", Proceedings of IEEE EMBC 2014.

3 Zheng C, Sato T, Kawada T, et. al., "Vagal nerve stimulation markedly improves long-term survival after chronic heart failure in rats.", Circulation 2004; 109:120–124.